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How does the brain work?

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7 Sep 2019,

UM Hemisphere Institute

Table of Contents

1)We know

- Anatomy
- Electrical Activity
- Bio chemistry

2)Goals of theoretical Neuroscience

- Identify Areas responsible for different functions
- Brain Mechanism vs behavior/cognition/emotions
- To understand how does the brain works?

3)My Targets

- Synchronization and composionality
- Numeration in the Brain
- From Neuro to Finance
- Ethics of Brain Machine Interface
- Bio-medical Projects (Sleep disorder and Epilepsy)

We know

ANATOMY

- Different sections of the brain
- 10^10 neurons
- Axon and dendrites
- Dendrites travel far
- White stuff
- Some localization of functions

ELECTRICAL ACTIVITY

- Synapses

BIOCHEMISTRY

- Neurotransmittors (Biochemistry)

We DON’T know:

- Precise location of cognitive/emotional functions

- Cognitive and emotional functions representation in the brain
  - Language mechanisms
  - Numeration representations
  - Mathematical skills
  - Musical skills

- How does the network works as a whole ?

  Which neuron “speaks” to which neuron?
  What are the rules?
  How to handle huge (!) amount of data

….

Trying to understand how does the brain works we localize the problem to

Neural Network

= a set of neurons with

an action and rules

“How does the brain work?”

which is still the

most intriguing question for the 21st Century!

Mathematical Methods from

- Dynamical systems
- Stochastics
- Wavelets

- Singularities
- Geometric Data Mining
- Statistics
- Probability

- Moduli of algebraic surfaces

We start with Brain Imaging

Imaging =

Recording device

plus a

Forgetful functor

plus a

Cleaning mechanism

Imaging Techniques

- Inter cellular recording
- EEG
- MEG
- PET SCAN
- fMRI

Advantages of MEG over EEG

- No touch
- 248 channels
- Easy to connect
- Not disturbed by the scalp
- One can use him/herself as a subject

Disadvantages

- No touch
- One cant use monkeys (need to be still)
- Not detecting radial current
- Low signal to noise
- 3MEuro

BIU MEG

- 248 Magnetometewholehead MEG system (WH3600, 4D)
- Simultaneous EEG recording
- Eye tracking
- A complete set of stimulation systems
- The MEG is inside a double wall magnetically shielded room by IMEDCO
- Cleaning and maintenance by Moshe Abeles/Squids, ect

What imaging devices do I use?

THEORY

SINCRONIZATION:

Inter Cellular recording on primates

Musical skills, Numeration, mathematical skills, metaphors:

MEG (and fMRI)

BIO-MEDICINE

Epilepsy: EEG, EEG under scalp

Sleep Disorder: EEG plus

ADHD in rats Inter Cellular recording

Students that contributed

Mina Teicher

יקי שטרן

לילך אביטן

אורי ירושלמי

יקיר ברצ'נקו

אמיר קלקס

תומר גזית

ענבל לוטוס

יואל פנחס

אורן שמיאל

A.
First proof of
Synchronization
in behaving animals

Conjectures on the way the Brain activity works

- Caos , firing rates , placticity
- Synchronization
- Compoisionality
- Synfire Chains

Spikes Synchronization and Hand Motion

- **Moshe Abeles**
- **Mina Teicher**
- **Tomer Shmiel**

Goals

Finding (unknown) relationships between hand-motion and brain-activity which are **NOT** induced from the population vector (frequency and direction ($\Sigma f_i v_i$))

We will focus on accurate spike patterns using computerized methods

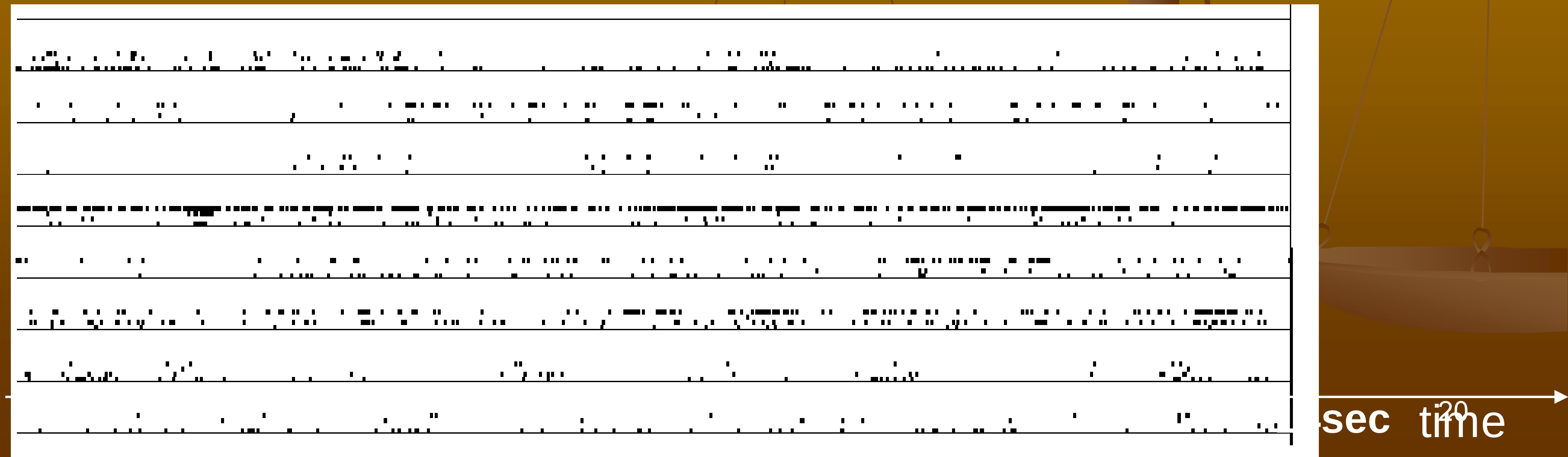
The Experiment:

Sampling Monkey's Drawings

Drawings by manipulandum are sampled at 100Hz

The Experiment:
Recording Neural Activity

- Recording brain activity using 8 micro-electrodes inserted under the scalp into the motor (and pre-motor) cortices
- Identifying stable individual neurons
- Spike-sorting for separating the electrical signals from each electrode to different neurons
- The data still contains spike noise



We are also interested in the Strength of a Relationships

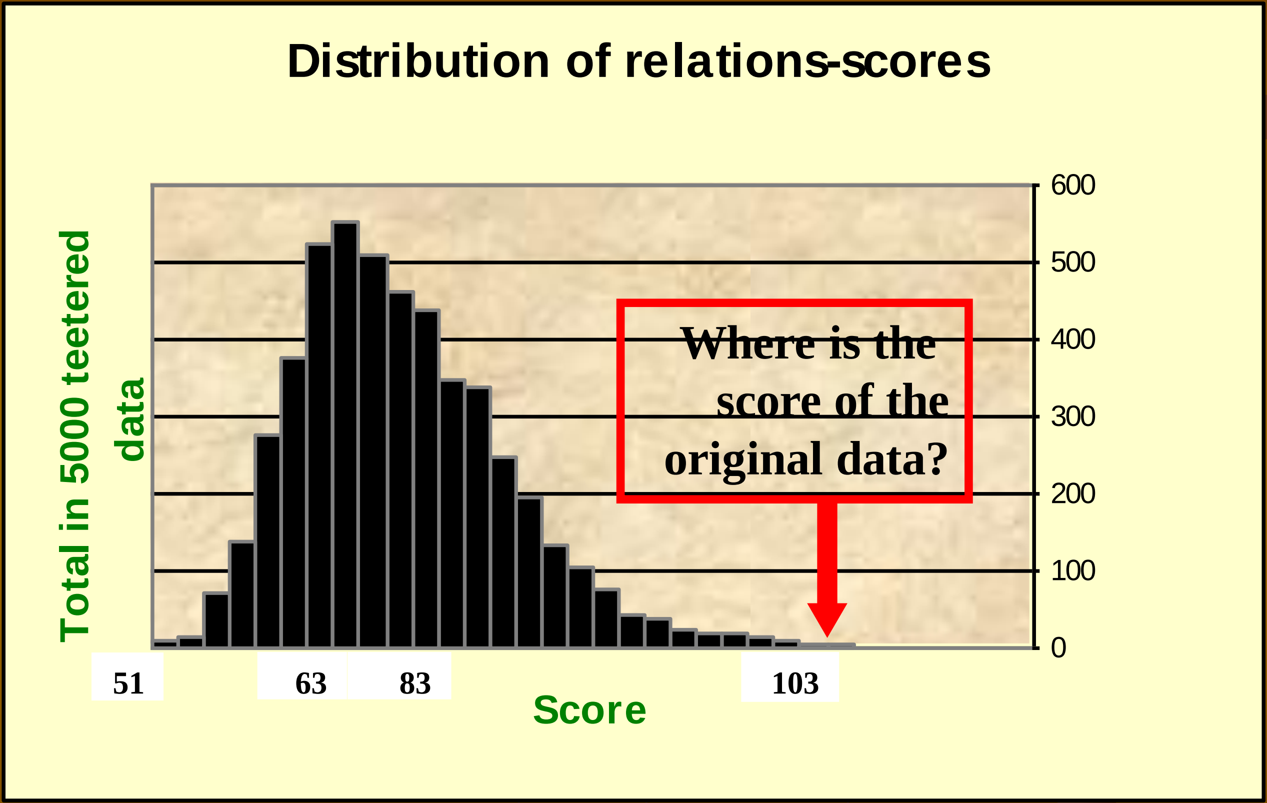
To each experiment day we give a "score "

(in a numerical value) that gives an estimate measure to the precise correspondence (synchronization) between activity and brain

This is done in 7 steps

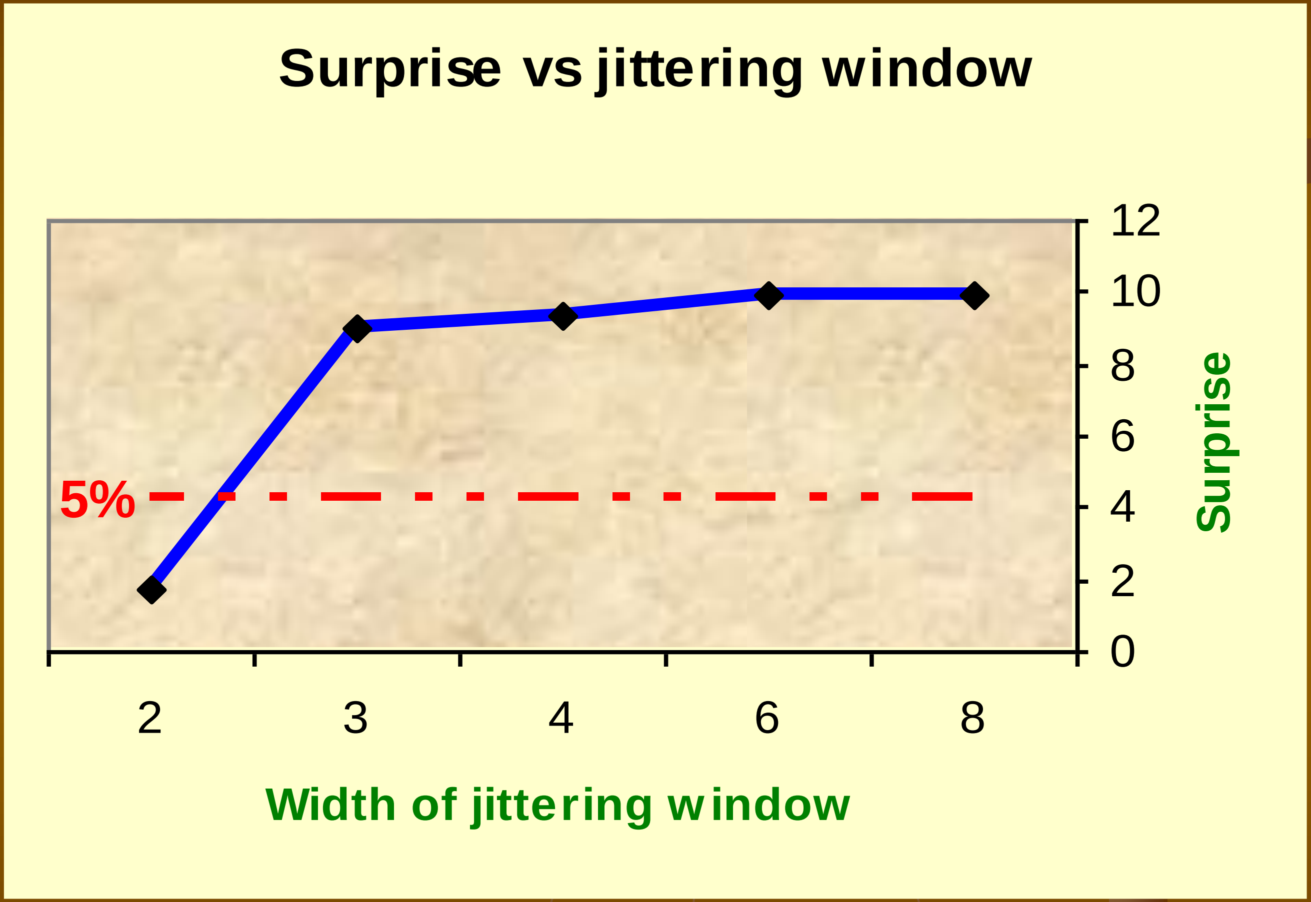
Results

(jittering-window used: 10ms)



None of the 5000 jittered data has reached the original score!!!

Results (cont.)



Significance of 0.2% for jittering window=3ms

Conclusions

Spikes hold information in a time resolution of 3 milli-seconds

This information seems to be related to the hand-motion direction and velocity

B. Numeration
Work in Progress

Ahmad Sleman

Amir Kleks

Yael Eisenberg

Mina Teicher

Is there a concept of a number in the brain?

- Initial steps
- Via MEG We try to find a common phenomena or a common location in the brain for no 3 as reaction to

- See 3 circles
- See the figure 3
- Hear 3 bips
- Feel three nocks

The picture can't be displayed.

Is there a concept of a number in the brain?

Plan to record MEG data from

- 20 subjects
- 100 experiments for each

So far

- 4 subjects
- 20 experiments for each

Is there a concept of a number in the brain?

Plan to use on 4D MEG the recording :

- Cleaning
- Matlab
- SAMBeamforming
- Data Mining

BIU Method for cleaning

Cleans the data of 50Hz+ harmonics

based on line side recording

Cleans the building vibrations

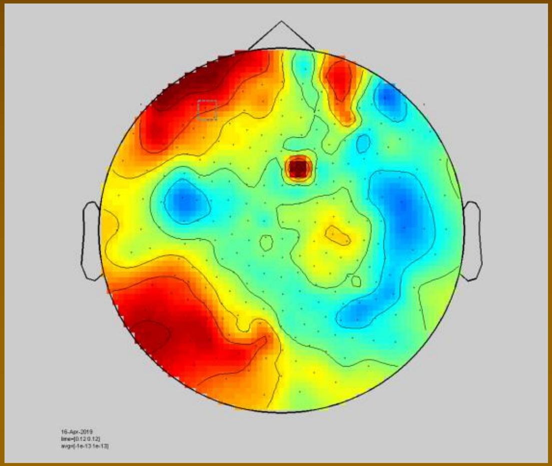
based on accelerometers recording

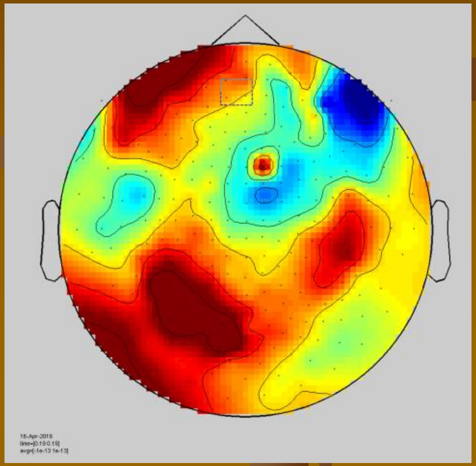
Cleans the data

based on reference channels

Applying different sets of weights

for different frequencies


16-Apr-2019
time=[0.12 0.12]


16-Apr-2019
time=[0.19 0.19]

Some open question in consultation with linguistic experts

1) is there a common location for THREE and THIRD?

2)What about 3 in Sign Language ?

C. Ethics of Brain Machine interface

- Work in Progress
- Short version published in Nature letters 2018

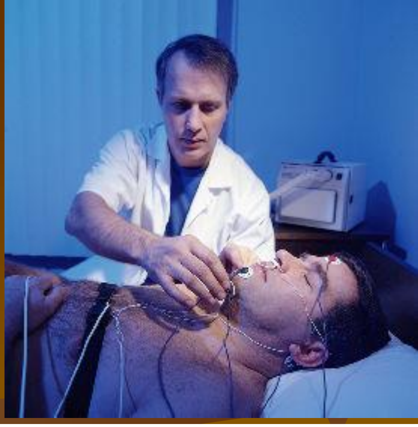
D. MEDICAL PROJECTS
- Sleep Disorders

Recognition of Sleeping Phenomena

- Prof. Yaron Dagan, Sleep Laboratory, TH Hospital and my PhD student Oren Shmiel

- we produced a way to predict sleep arousals from synchronized channels

The Experiment:



Simultaneous measures of the following channels:

Channel	Description	Sampling (Hz)
EEG	מוח	100Hz
EOG	עיניים	100Hz
EKG	לב	200Hz
EMG Submental	שרירי סנטר	200Hz
EMG tibialis	שרירי רגליים	200Hz
Pulse	דופק	1Hz
SaO2	סטורציה (ריווי חמצן)	1Hz
Air Flow	נשימת אף	10Hz
Thorax, Abdomen	בטן וחזה	10Hz
GSR	מוליכות העור/הזעה	200Hz
Snore	נחירות	200Hz
Position	תנוחת גוף	1Hz

Goals

1) Prediction of **pre-sleeping behavior** from channels which can be recorded easily

2) Prediction of **arousals** in channels which can be recorded easily.

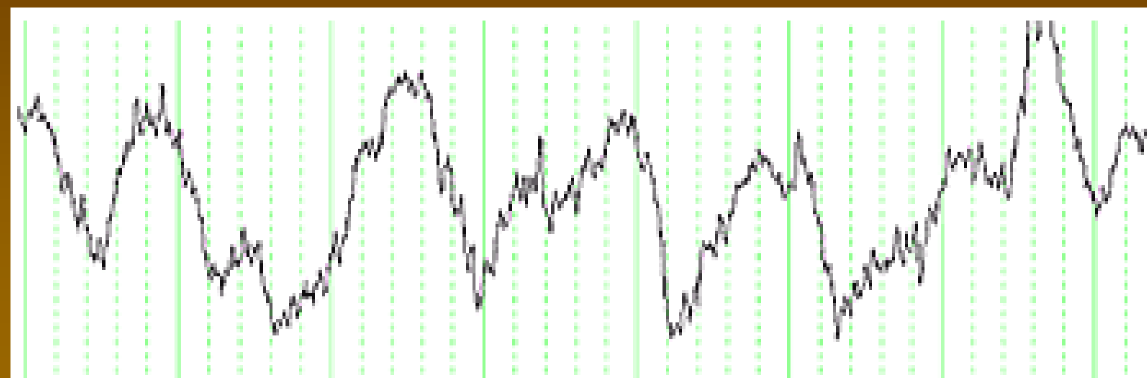
3) Relationships between the **GSR and other channels (especially EEG, EOG, EMG).**

EEG Recordings in Sleep Research are classified by:

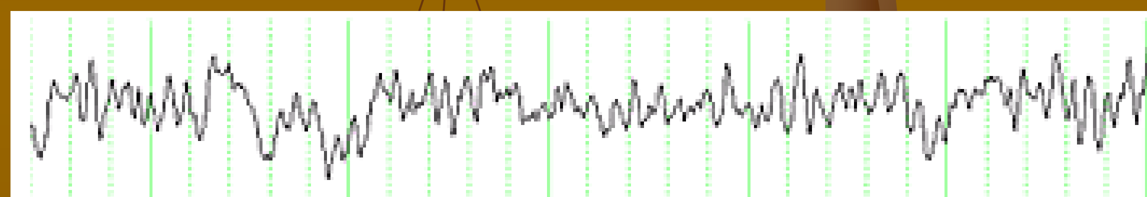
- Frequency (Cycles/Sec = Hz).
- Amplitude (Voltage).
- Shape and structure.

EEG Frequency in the different sleep phases

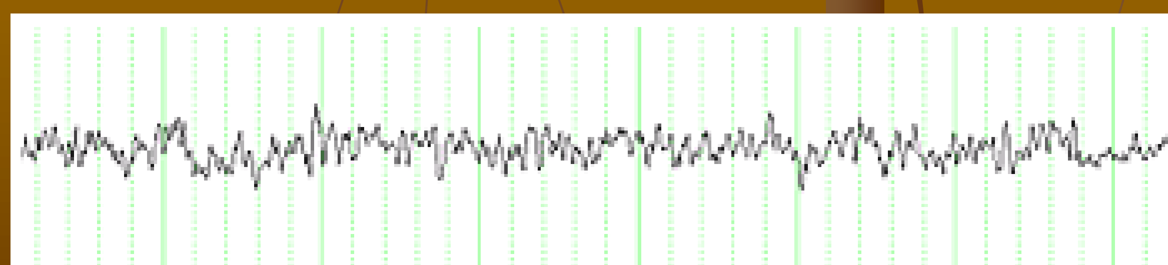
Delta (0-4 Hz)



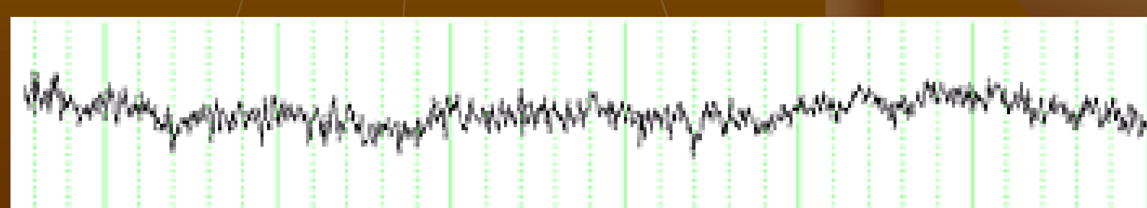
Theta (4-8 Hz)



Alpha (8-13 Hz)

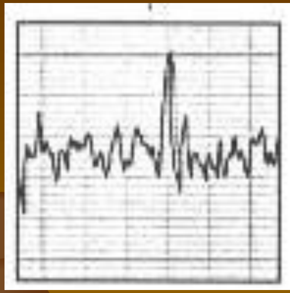


Beta (> 13 Hz)

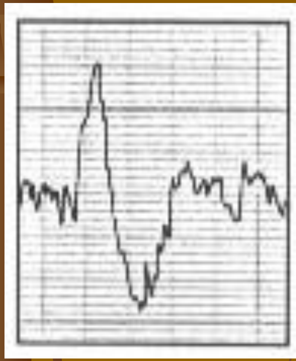


EEG Shape and structure

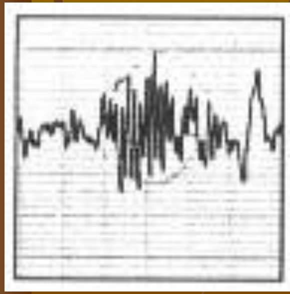
Vertex Waves: Sharp negative waves.



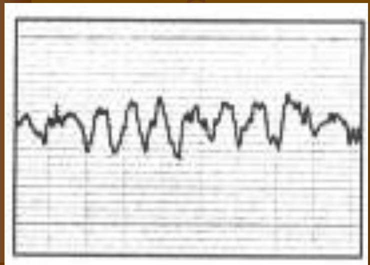
K-complex: A sharp negative wave followed by a slower positive component.



Sleep spindles: Short clusters of 12-14Hz.



Sawtooth waves: Low amplitude, saw tooth appearance.



Sleep Stages

Stage 1:

- Low amplitude mixed frequency in EEG.
- Vertex waves (at late part) in EEG.
- Slow eye movements in EOG.

Stage 2:

- Sleep spindles and K complexes in EEG.

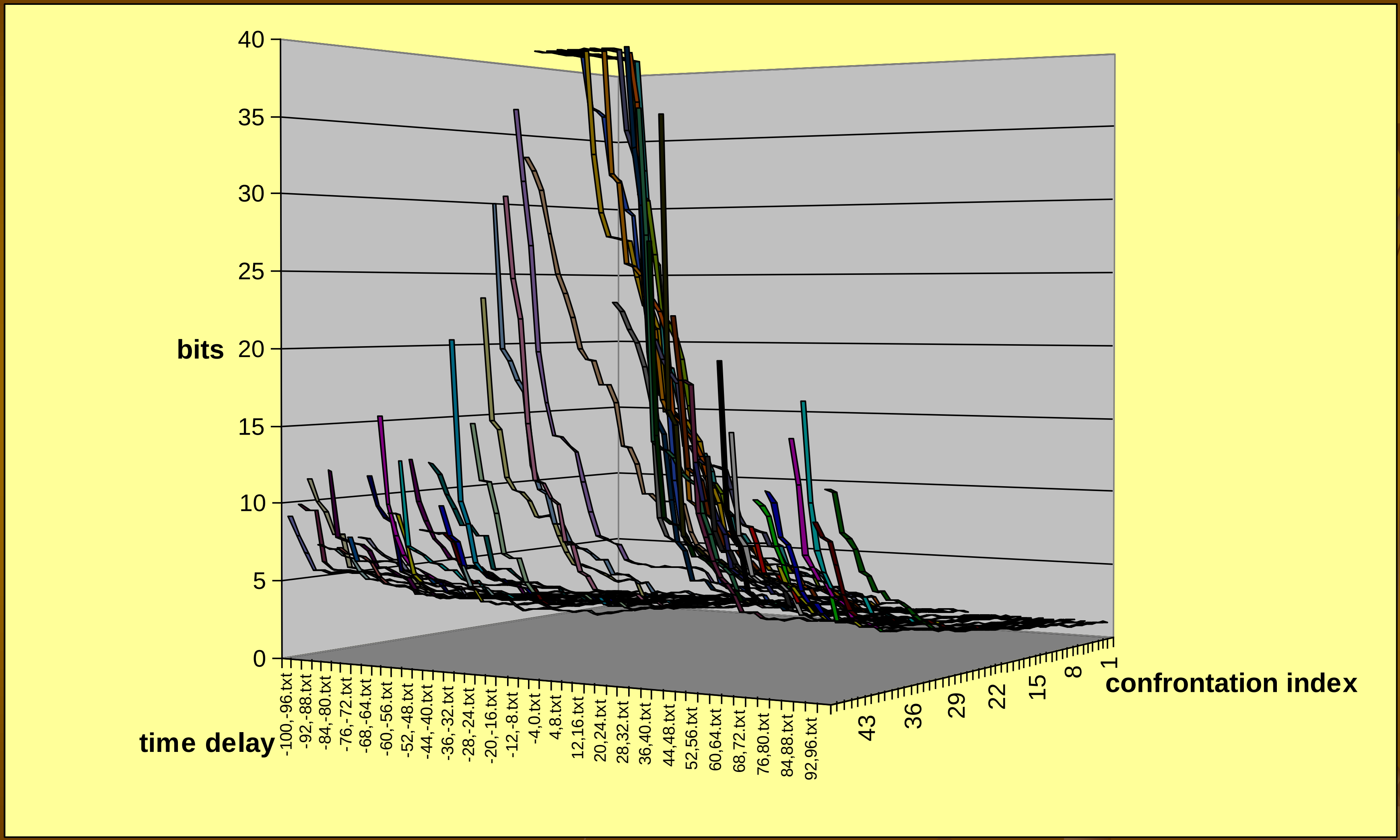
Stages 3,4:

- Delta waves with high amplitude in EEG.

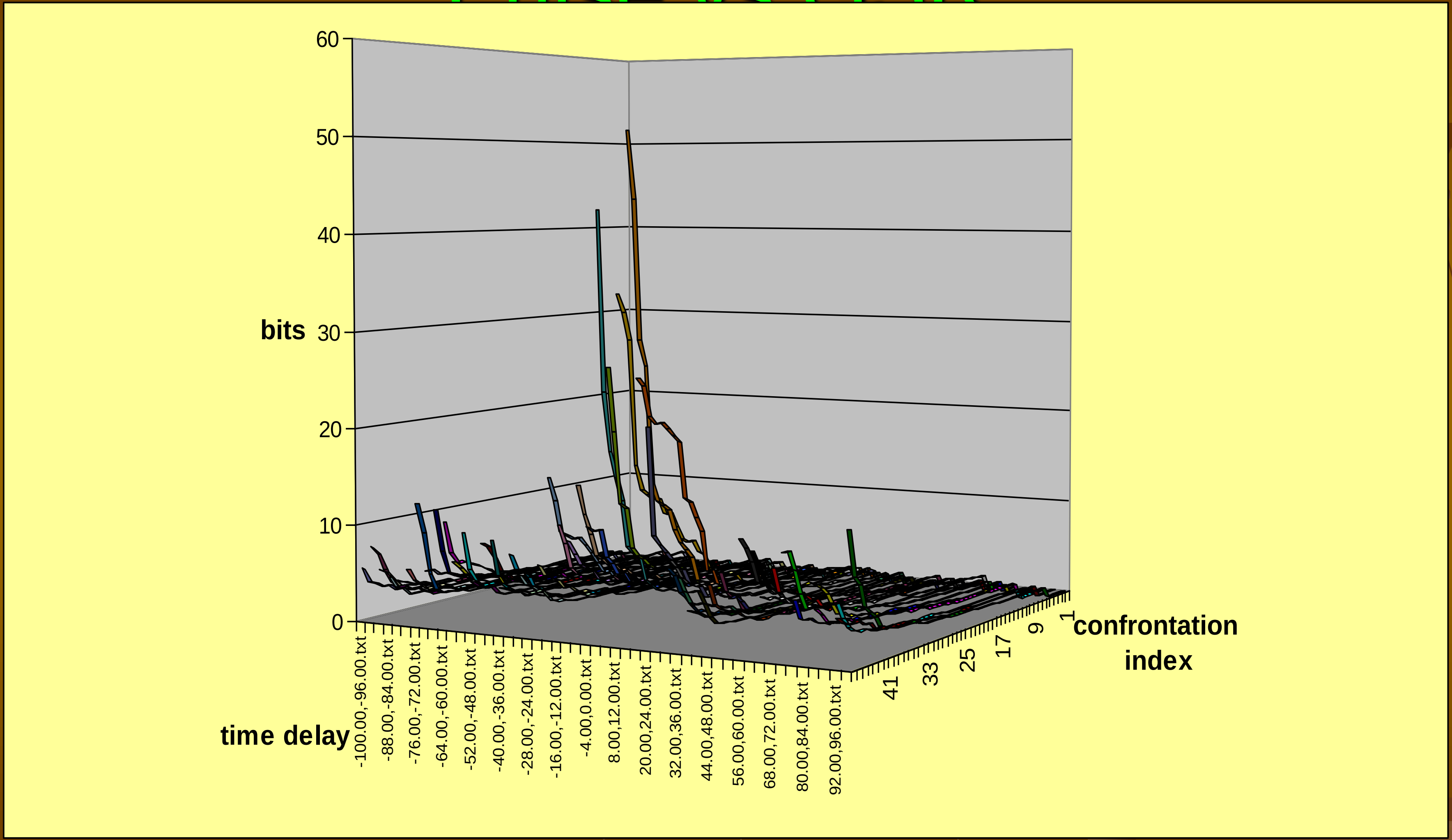
Stage REM:

- Segments of Rapid Eye Movements in EOG.
- Low amplitude, mixed frequency in EEG.
- Saw tooth waves seen in many patients in EEG.
- Decrease in amplitude to the lowest level in EMG.

Preliminary RESULTS: Pulse vs SaO2



Preliminary RESULTS: Pulse vs GSR



In Progress:
: Detecting Arousals

Computerized method to identify arousals
from
EEG, EMG, Pulse, Saturation

E. From Neuro to Finance

We extend and ask what is the common to the below Examples

a. Financial Markets
b. The Brain
c. Cities and Transportations
d. Health Systems

They are all Complex System!

What is **A Complex System?**

A collection of individuals

whose behavior affects the total in a way which is unclear to the observer

The parts are interdependent.

So pushing on a complex system "here" ,

often has effects "over there‟

It involves Multi Scale Hierarchies ,

Indeed, the below systems are made of individuals:

Social systems formed (in part) out of people,
the brain formed out of neurons,
molecules formed out of atoms,
the weather formed out of air flows,
the financial market formed out out traders

Understanding Complex Systems

* **indirect effects**. (causes and effects are not obviously relate
* how **interactions** give rise to patterns of behavior
* **how its parts give rise to the collective behavior**
* how the system **interacts with its environment**
* their **Multi Scale Hierarchies**
* the process of formation complex systems through (geometric and algebraic) **pattern formation and evolution** .

Building tools

Conceptual – for building concepts that help us think about these systems

Analytical - studying these systems in greater depth, and

computer based - for describing, modeling or simulating these systems.

In summary

- Cause and affect
- Multi Scale hierarchies
- Interactions
- Evolutions

Are common to all above examples and in particular to the brain and the financial markets

The goal is to transfer methods and discoveries **from Neural Computation to Mathematical Finance**

F. Localizing Epileptic Activity

Esther Adi-Japhe
Mina Teicher
Amir Zilberstein
Tomer Gazit

D. Kippervase (Ichilov Hospital)
Miri Neufeld (Ichilov Hospital)
Itzik Fried (Ichilov and UCLA)

Epilepsy is :

- A prevalent neurological disorder
- Characterized by abnormal excessive neuronal activity termed seizures
- An epileptic seizure originates in an epileptic focus located in an epileptic zone
- When medications fail, a surgery is considered in which one needs to locate the epileptic zone
- Surgery is considered when the patient has only one epileptic focus

We produced three accurate Inverse algorithms to localise epileptic focus

- If there is an agreement between the EEG raw data and MRI anatomical findings operation can be done
- If there is no agreement among the 2 data's then our algorithm will determine, and eliminating the need of a very invasive operation
- In this talk we elaborate on one of the Inverse algorithm – the Genetic Algorithm
- The inverse algorithms is basedfllows measurement and preprocessing

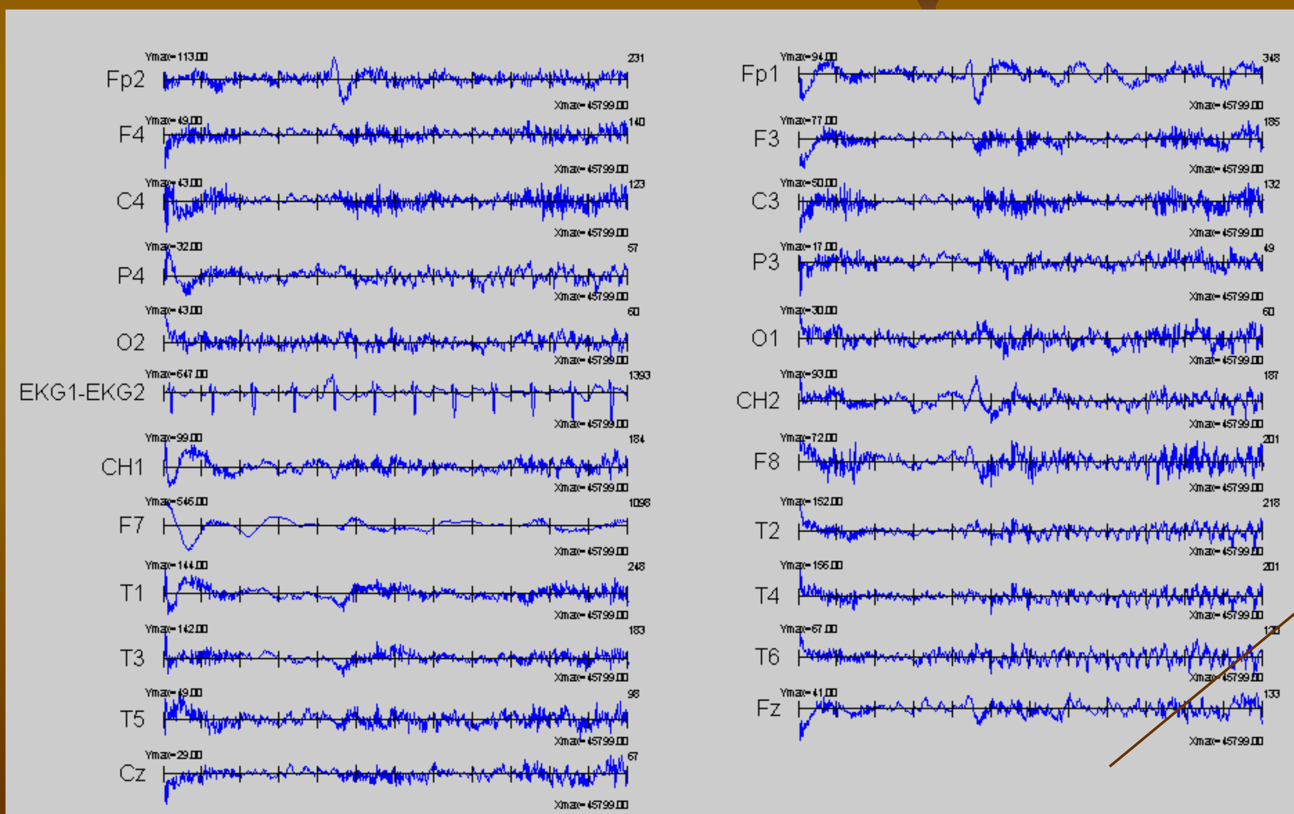
Steps in Localizing the Epileptic zone:

1. Obtain seizure measurements
2. Pre-processing
3. Inverse Algorithm (incl. Brain Model)
4. Compare results with pathology

We are improving almost all parts of the process (especially the green..

1.Obtained seizure measurements

An automatic tools to automatically find a segment of EEG recordings that appears in the beginning of an epileptic activity



2. Preprocessing

- Clean Noise using events contradicting the Dipole fit Model and other methods.

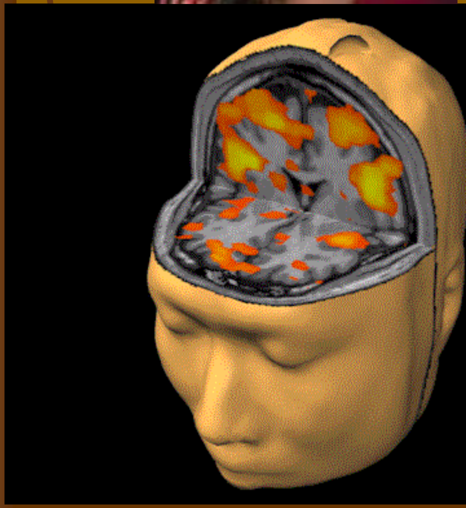
- Calculate the "Amount of Epilepsy" for every electrode ("replacing Amplitude")
  - The EEG of the event is not characterized by a fixed "shape"
  - Epileptic source can be seen over relatively large time scale

3. INVERSE EEG Algorithm

We look for N dipoles which we believe that they formed the EEG measurement for a specific timestamp

We developed three algorithmic approaches for:

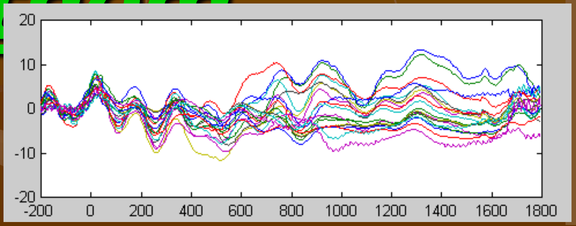
- Mapping 3D electrical brain activity
- Finding the location of an interesting phenomena (like epilepsy)



A. ***Genetic Algorithm***

B. ***Analytic Algorithem***

C. ***Wavelets***

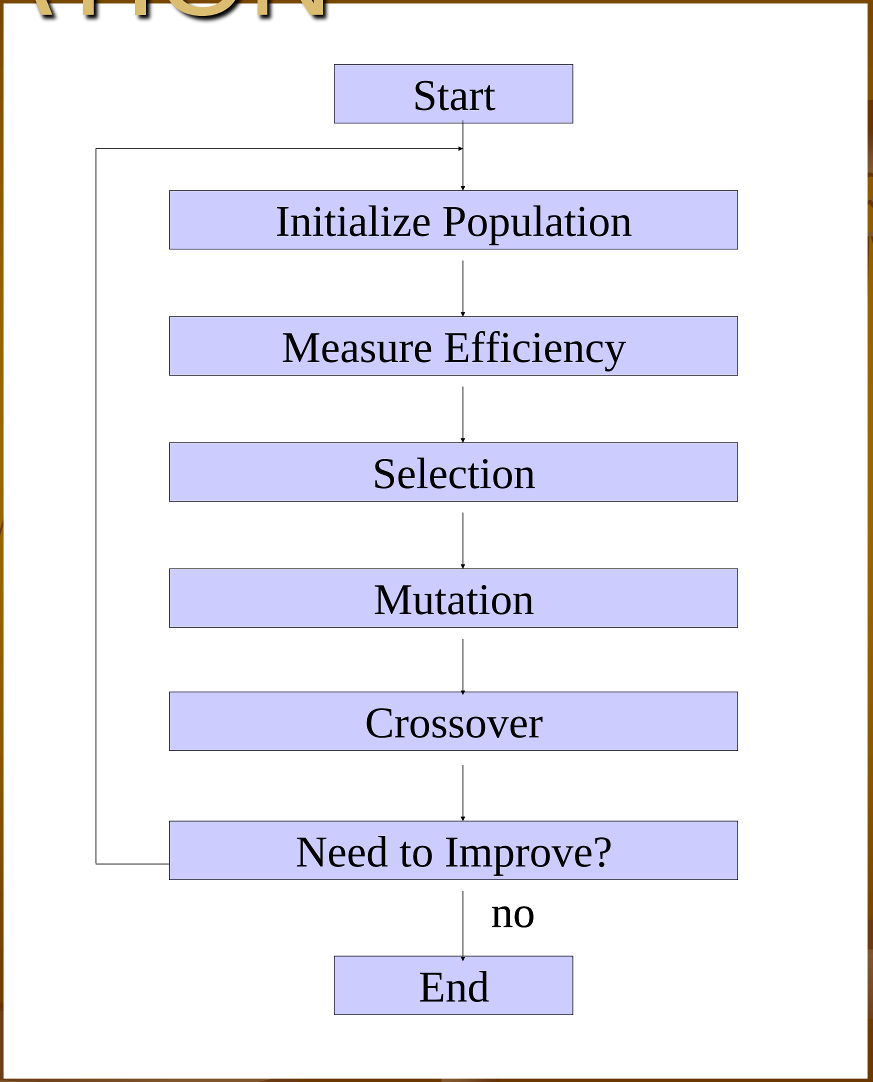


A. INVERSE EEG Algorithm based on GENETIC Type ALGORITHM

- Genetic algorithms are search algorithms- they are stochastic algorithms, which is a sub-class of Randomized Algorithms
- based on the mechanics of natural selection and natural genetics (Goldberg 1989)
- It consists of 3 steps:

Selection, Crossover, Mutation

Genetic Algorithm- SUMMATION



The adaptation:

1. Our adapted Modification take time frames of Epilepsy into account

The solution depends also on:

2. Measurement properties

Number of electrodes

Electrodes locations

3. Head model choice

Find simplified models (computationally feasible) for the relation between brain activity and scalp potentials

4. Source model choice

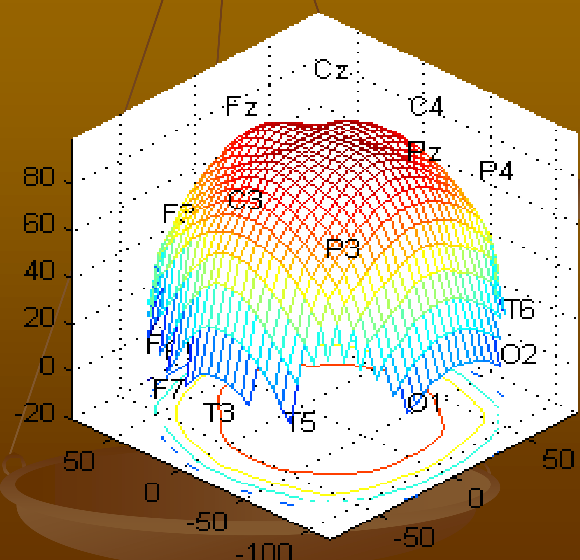
Brain activity properties

5. Noise

2. Measurement properties

- Number of electrodes

- Electrodes locations



Central
Frontal
Occipital
Parietal
Temporal

3. Head Models

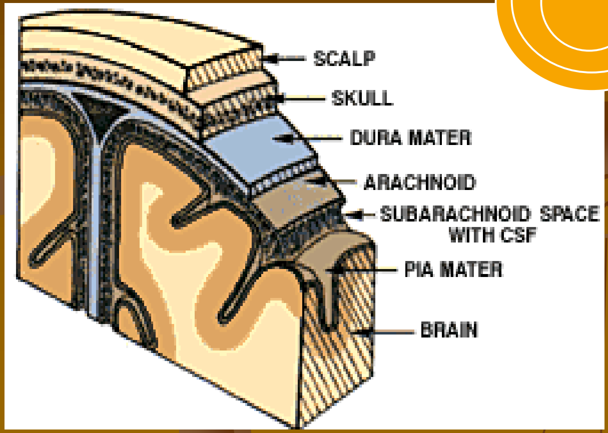
We use 3 types of Head Models for our Forward Computations for EEG

3.1 Layered Head Model

3.2 Realistic Head Models

3.3 Geometric Realistic Head Models

3.1. Layered Head Model



De Munck and Peters 1993

- Properties:
  - Set of concentric spheres
  - Homogeneous conductivity in every layer

Layer	External radius [mm]	Conductivity [S/m]
Scalp	76.49	0.33
Skull	71.76	0.0042
CS fluid	64.03	1.00
Brain	61.53	0.33

*Conductivity and radius measurements from ***Ferdjallah 1996***

Layered Head Model

Formula for Potential on the Sculp

$$v(r) = \frac{1}{4\pi} \sum_{j=1}^{m} (\sigma_j^- - \sigma_j^+) \int_{G_j} J(r') \frac{r - r'}{\|r - r'\|^3} dr'$$

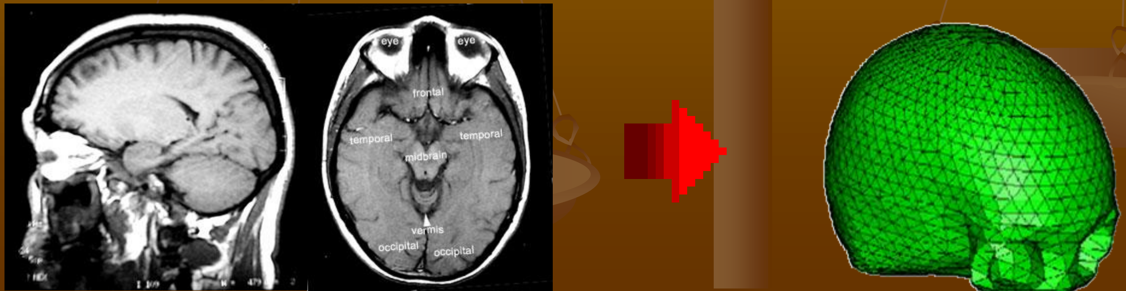
m	Number of layers
σ_j^-	Conductivity inside layer *j*
σ_j^+	Conductivity outside layer *j*

- *Disadvantage of the Layered Head Model :*

  Using Perfect Spheres which cannot cover all head areas

3.2. Realistic Head Models (RHM)

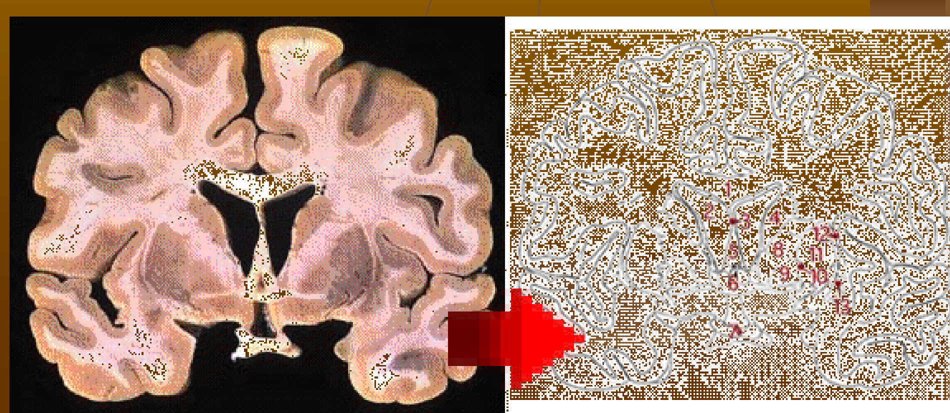
- INPUT: MRI/CT scan (1mm between each cut)
- 2D realization (using differential methods) of the input
- Surface/3D segmentation with equal triangle elements each with its conductivity (equal number o triangles in each layer)
- Interpolation of measured conductivity (between the initial slices)
- Numerical solutions for (Conductivity dependent) Forward Computation (e.g: BEM - Boundary Element Method). (determining potential on the scalp from assumed sources of a specific activity)



3.3. Geometric Realistic Head Model (GRHM

3D realization of the brain

obtained from the given set of MRI pictures using **Image Processing** (inc **geometrical edge detection**) corresponding to the shape to the internal surfaces.



3.3 Geometric Realistic Head Model (GRHM

(cont)

Giving

a segmentation

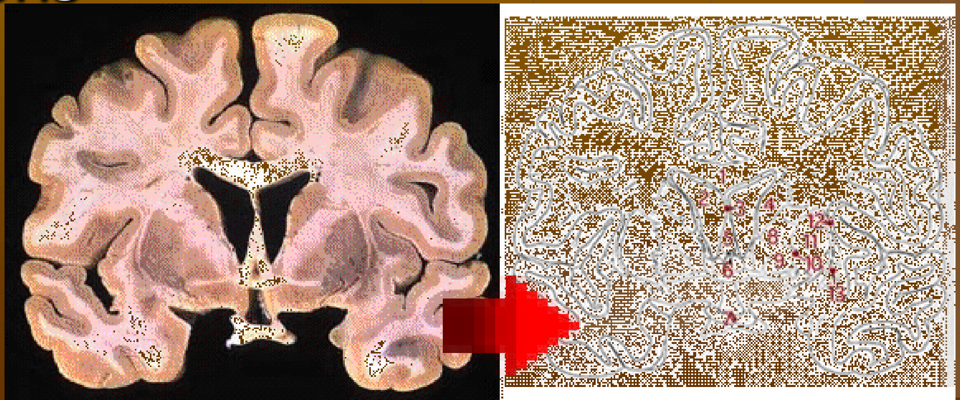
with no equal number of elements in each layer

with different shapes , (not necessarily triangles)

With resolutions which do not depend on other layers.

Advantages:

Resolution Cortex and Dipole Orientation are normal to each other, so we can use this in the model to avoid 'bad' solutions



4. Source Models

4.1 Dipole Source Models

4.2 Distributed Source Models

4.3 Improved Source Models

4.1 Dipole Source Models

- Look for the best choice of few dipole(s) position(s) and orientation(s)/amplitudes(s)

Dipole source properties:

- Location: $r' = (r'_x, r'_y, r'_z)$
- Moment (Orientation) : $J(r') = (J_x, J_y, J_z)$

- under search, which is guided by minimization of a cost function - matching the Forward Computations with the input (EEG measurements).

4.2 Distributed Source Models

- Evenly spread fixed locations in the whole brain volume (or on the cortical surface).

- Look for the best choice of amplitudes (and/or orientations) for each location

5.Noise

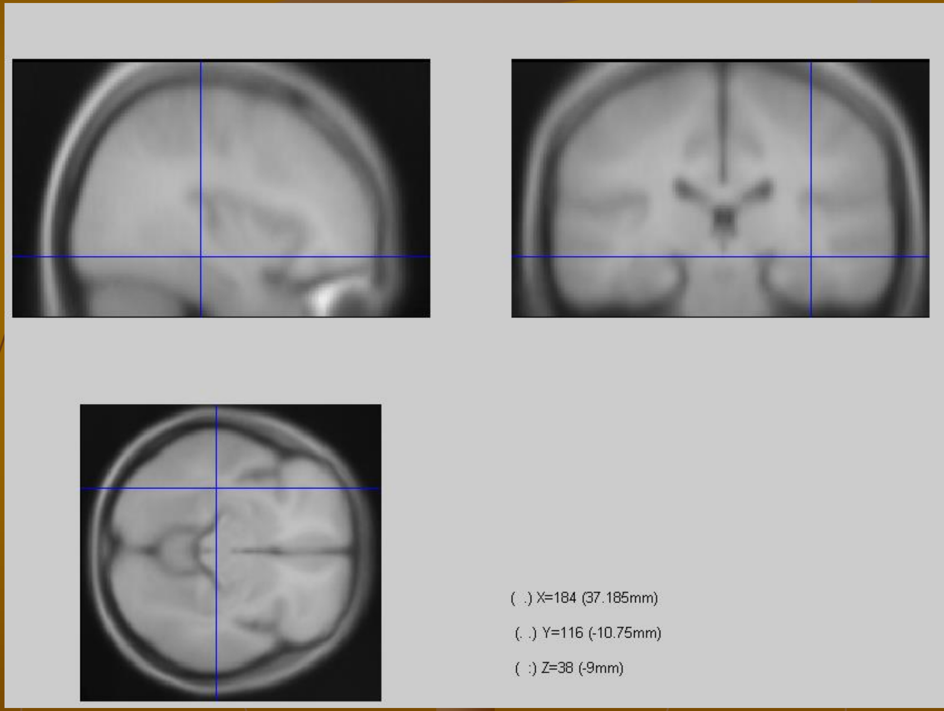
- Environments noise
- Additive noise on sensors
- Brain background activity
- Physiological (motoric) artifacts

We tested the Genetic Algorithm on simulated data

- Several different head models
- Several different source configurations- simulation
  - Predefined event area/areas
  - Event area/areas activity is simulated using averaged ERP trials
  - Other areas activity is simulated using randomly chosen EEG segments
- Use Forward Computaion related to the head model to calculate the electrode 'measurements'
- Add white Gaussian noise to 'measurements'
- Data SNR (Signal to Noise Ratio) is known and can be controlled

Comparing Results (Real Data)

- temporal lobe patients
- Candidates for surgery
- Results were in accordance with pathology



B. Inverse EEG solutions based on Distributed Source Models

Notations

- N_V - # of sources
- J - Vector of source amplitudes
  (known locations)
- N_E - # of measurement points
- Φ - Vector of amplitude measurements
  (known locations)
- K - Lead Field Matrix determining a linear Forward Computation

Notations - cont

- K is matrix of size $N_V * N_E$
- Example for K: $k_{\alpha\beta} = k(r_\alpha, r'_\beta) = \frac{1}{4\pi} \frac{(r_\alpha - r'_\beta)}{\|r_\alpha - r'_\beta\|^3}$ (1 layer, conductivity 1)
- For noise free measurements: $\Phi = KJ$

Remark

- Note that since $N_V > N_E$ there is an infinite number of inverse solutions

Existing Inverse EEG solutions based on Distributed Source Models

- MNE - Minimum Norm Estimates (*Hamalainen and Ilmoniemi, 1984*)

Search for the <u>minimum power</u> solution
(minimize the ordinary quadratic L2 norm)

Find J s.t, $\min_{J}\{\|\Phi - KJ\|^2 + \lambda\|J\|^2)$

The inverse solution is $J = K^T[KK^T + \lambda I]^{-1}\Phi$

- LORETA - Low Resolution Brain Electromagnetic Tomography
  (R.D. Pascual-Marqui et al., 1994)

Search for the <u>smoothest</u> solution
(minimize the Laplacian of the depth-weighted current distribution)

Improved Distributed Source Methods

- Former distributed source solutions ignore the time domain
- Goal: Force smoothness of sources over time which vanish over polynomials of a given degree.

- UNDER A PATENT APPLICATION …..

The End

One more slide

Speech Recognition

Acoustic Detection of the Red Palm Weevil Based on Speaker Recognition Paradigm

Automatic Acoustic Detection of the Red Palm Weevil,
In “Computers and electronics in Agriculture” 2008
Y. Pinhas, V. Soroker, A. Hetzroni, A. Mizrach, M. Teicher, J. Goldberger